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Epilepsy and injury mortality in Sweden—the importance of changes in coding practice

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We analysed national mortality trends of injuries and poisoning in patients with epilepsy to establish the importance of changes in coding practice. Patients where epilepsy was a syndrome, either as an underlying or contributing cause-of-death at any time of life, throughout Sweden during 1975–1995 were included. All conditions mentioned on each death certificate were examined, and epilepsy and injury diagnoses were separated according to underlying, contributing or multiple cause-of-death. Annual mortality rates, case-fatality rates, and linear regression coefficients were computed. The most common underlying cause-of-death (UCD) was diseases of the circulatory system (34.4%) followed by epilepsy (31.7%). Injury and poisoning were coded as UCDs for 5.8% of the patients. Injury and poisoning as a contributory cause-of-death increased significantly, but not as an underlying cause during the study period. The proportion of each diagnostic group as an underlying cause decreased by 35% for epilepsy and 18% for injury from 1981 and onwards. These changes should be interpreted with caution since changes of coding practice are more likely to be the cause of these apparent changes. The most frequent specific external causes of injury deaths in epileptic patients were falls and drowning. Intracranial fatal injuries in connection with fall accidents predominated, especially among elderly persons. Deaths related to accidental poisoning were caused by the toxic effect of non-medicinal substances. Cause-of-death statistics from different countries must be interpreted with caution when making international comparisons. Both underlying and contributing cause-of-death statistics should be considered in analyses of mortality trends.

Key words: epilepsy; mortality; accidents; injury; standardized mortality ratio; epidemiology; cause-of-death.

INTRODUCTION

Epilepsy is estimated to affect approximately 50 million people worldwide[1,2]. Up to 30% of patients with refractory epilepsy do not have remission despite appropriate therapy with antiepileptic drugs[3–5]. One fatal outcome of an epileptic seizure is injury—especially fall injury, burn and suffocation including drowning[6]. Several studies of cause-specific injury mortality rates in patients with epilepsy show a similar pattern[7–15]. Observed deaths from injury and poisoning are reported to be five times greater among epileptics than that expected for the population at large[7]. Severe injuries include intracranial trauma, skull fracture, burn, and drowning. The most common bodily site of a fatal injury is the head[16]. Although most patients with minor problems have an injury risk equal to the total population, including children[17], one third of epileptic patients are injured during seizures[9,16].

Only a few longitudinal studies have focussed on the specific mortality pattern, including suicides and violence[7,12,23]. However, analysis of injury mortality data on underlying cause-of-death (UCD) in epileptic patients is of limited value due to the low case-fatality ratio. Thus, all conditions mentioned on death certificates for the entire Swedish population have to be analysed.

The aim of the present study was to analyse: (i) the longitudinal trend in the Swedish national mortality rate among persons with epilepsy and injury diagnoses, including all conditions on death certificates concerning underlying, contributing or multiple cause-of-death; (ii) the nature and external causes of injury and poisoning in epileptic patients; and, (iii) the influence on time trends of epilepsy

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and injury mortality in relation to the adjustment of registration practice of the Swedish cause-of-death statistics.

MATERIALS AND METHODS

Design

A national longitudinal study of mortality caused by unintentional/intentional injury and poisoning was performed of persons with epilepsy during the period 1975 to 1995.

Study population and area

Patients where epilepsy was a syndrome, either as an underlying or contributing cause-of-death during any time of life throughout Sweden during 1975–1995, were included in the study.

Swedish cause-of-death statistics

The Swedish death certificate is based on the 'international form of medical certificate of cause-of-death' adopted by the WHO, on which conditions contributing to a death are reported in two sections (parts I and II). In part I, the certifier is asked to state the final complication that eventually led to death, and the sequence of conditions leading up to it. Thus, the UCD, i.e. the condition that initiated the train of events leading to death, is reported on the bottom line in part I. In part II, the certifier should state any other conditions contributing to a fatal outcome but not related to the sequence reported in part I.

The eighth revision of the international statistical classification of diseases, injuries, and causes of death (ICD-8) was used in Sweden from 1969 to 1986. In addition to UCD, up to six complications or contributing causes were recorded. The ninth revision (ICD-9) was introduced in 1987, and from that year onwards, all causes-of-death on the death certificate, up to a maximum of 33, have been recorded[19, 20]. Coding is performed centrally at Statistics Sweden in Stockholm. From 1987 it has been possible to identify immediate cause-of-death from the death certificate.

Adjustment of registration practice

In the 1970s, it was found that selection of UCD had not been consistent, which resulted in important artificial trends in published statistics. A review of the registration practice showed that the selection of the UCD was not always the result of a strict application of the ICD selection rules, but rather in some cases a reflection of what the coders felt to be the most important condition reported on the certificate. In response to this review, a set of supplementary coding instructions was developed. The new coding instructions aimed at increasing the reliability of the registration procedure and a greater compliance with the ICD rules, so that the condition reported by the physician as the UCD was also more often registered as such in the cause-of-death register. From the data-year 1981 and onwards, the registration practice of the Swedish cause-of-death statistics was adjusted. In general, but not always, this meant a closer adherence to the instructions included in the ICD[21]. A specific follow-up of the contents of the first edition of the supplementary coding instructions comprised 18 diagnostic groups. Among 13 groups a significant change of trend was found following the predicted outcome of the altered registration practice[22]. The Swedish National Board of Health and Social Welfare decided to implement the ICD-9 version in Swedish health care from the year 1987.

Data collection

Data on mortality from injuries caused by external violence and poisoning (E800–999) and epilepsy (N345.00–99) during 1975–1995 were taken from the Swedish national cause-of-death register. All conditions mentioned on each death certificate were examined, and epilepsy and injury diagnoses were separated according to underlying, contributing or multiple cause-of-death.

The data were classified in four geographical regions in Sweden: Stockholm (1352 cases, 19%), Gothenburg (584 cases, 8%), Malmő (332 cases, 5%) and the rest of Sweden (4690 cases, 67%).

Coding error was found in a small number of cases. In the ICD-8 coding (1975–1986), E-coding was performed incorrectly for two patients, and information on the nature of injury was not available for another two patients. In the ICD-9 coding (1986–1995) the N-code was not available for one patient. These five patients were excluded from the analysis.

Statistical methods

Annual crude death rates from epilepsy were calculated from the total number of deaths where epilepsy was mentioned either as UCD or multiple contributing cause-of-death (MCCD) in patients with epilepsy during a year divided by the total population in that year multiplied by 100 000. Adjusted or standardized

mortality rates were based on comparisons with the general Swedish population in the year 1995. Case-fatality rates of epilepsy were calculated as the total number of deaths in a year divided by the total number of epileptic patients in that year multiplied by 1000. Case-fatality rates were standardized by taking 1995 epileptic patients as the standard population. Linear regressions were performed with the year of data as an independent variable and various mortality variables as dependent variables.

RESULTS

Distribution and specific causes-of-deaths in patients with epilepsy

In total, there were 6958 deaths from epilepsy (3359 deaths during 1975–1986, and 3599 deaths during 1987–1995). 4109 deaths were males (59%), and 2849 females (41%). Mean age at the time of death was 60.7 years (median = 65 years; range = 1–101 years). During the first study period, 1212 of the 3359 deaths (36%) were coded with epilepsy as UCD. The corresponding figure for the second study period, among 3599 deaths, was 993 (28%). For the rest of the patients, epilepsy was recorded as either the sole contributing cause-of-death or one among multiple contributing causes.

The most common UCD was diseases of the circulatory system ($n = 2394$; 34.4% of total) followed by epilepsy ($n = 2205$; 31.7% of total). Injury and poisoning were coded as UCDs for 405 (5.8% of total) patients. Other specific causes of mortality were respiratory diseases ($n = 503$; 7.2%), mental diseases ($n = 429$; 6.2%), neoplasm ($n = 323$; 4.6%), other nervous diseases ($n = 205$; 2.95%), diseases of the digestive system ($n = 123$; 1.8%) and others ($n = 371$; 5.3%).

Epilepsy mortality and case-fatality rates

Figure 1(a, b) shows epilepsy mortality rates per 100 000 inhabitants for 5-year age groups. Epilepsy as UCD shows two peaks. One was at about 35–44 years of age, the other at about 85 years. The overall death rate among patients with epilepsy showed a gradual increase with age, and peaked at about the age of 85 years. Figure 1(c) shows the age distribution (5-year categories) of injury and poisoning case-fatality rates in patients with epilepsy. Injury and poisoning mortality start to rise at the age of 20 years and peak in the age group 40–44 years.

Trend in mortality and case-fatality rates in epileptic patients

Table 1 shows summary results of the linear regression analysis, and Fig. 2 illustrates the scatter diagrams and trend lines of various age-adjusted mortality rates in relation to time. Epilepsy mortality (as an UCD) has not changed significantly over the last two decades (Fig. 2(a)). However, overall mortality (where epilepsy was coded either as an underlying or contributory cause-of-death) in patients with epilepsy increased significantly over the same period (Fig. 2(b)). By contrast, case-fatality rates in patients with epilepsy declined significantly over the last two decades, whether or not epilepsy was coded as an underlying or a contributory cause-of-death (Fig. 2(c, d)). Injury as an UCD in patients with epilepsy has not changed significantly over the last 21 years (Fig. 2(e)), but injury and poisoning as a contributory cause-of-death did show a significant increase (Fig. 2(f)).

Adjustment of Swedish registration practice

It was possible to calculate the ‘underlying cause proportion’, from the data set, i.e. the number of times a condition has been registered as UCD divided by the number of times it was mentioned anywhere on a death certificate, for all conditions investigated. Changes in the proportions may reflect changes in coding practice, which is shown in Table 2.

A change in trend was observed for epilepsy, and also for injury and poisoning. The proportion treated as an underlying cause decreased by 35% for epilepsy, and by 18% for injury and poisoning. This suggests that both epilepsy and injury/poisoning as an UCD has been replaced by other diagnoses as a result of change in registration practice.

Nature of injuries (ICD N-codes)

Intracranial injuries excluding fractures formed the most common category of cause of injury deaths in patients with epilepsy (29% during 1975–1986 and 21% during 1987–1995). Fracture (800–829) and poisoning by drugs, medicinal or biological substances (960–979), and toxic effects of non-medicinal substances (980–989) were the other most common causes of injury deaths. The most frequent scenario was for an externally caused fall to lead to fracture and intracranial injury. Deaths due to drowning were not specified in most cases. Deaths from accidental poisoning were sometimes due to the toxic effect of some non-medicinal substances. In Fig. 1(c) the distribution of all injuries is presented in 5-year age groups.

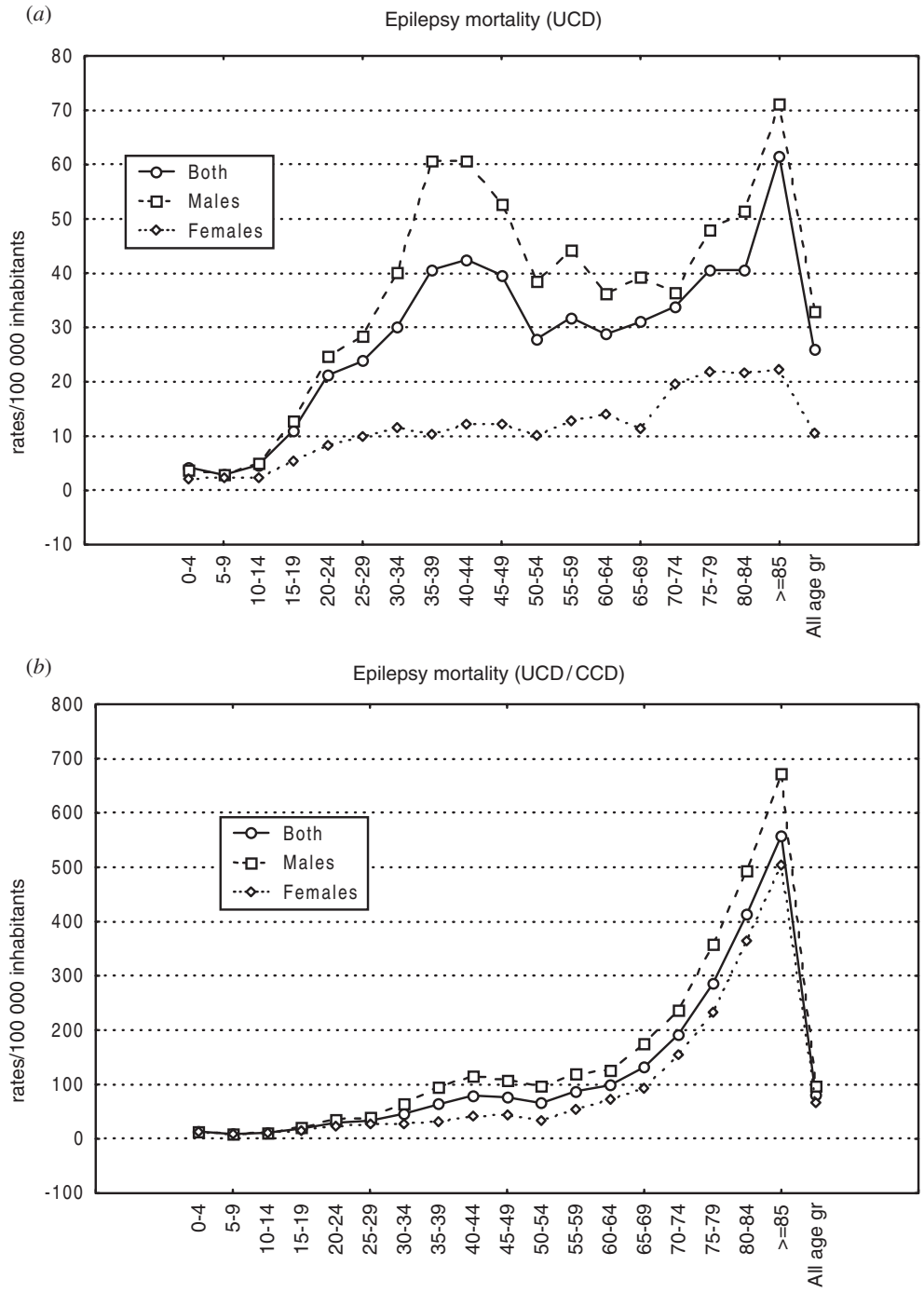

Fig. 1: Five-year age distribution of epilepsy mortality rates/100 000 inhabitants (Fig. 1(*a*,*b*)), combined injury and poisoning (Fig. 1(*c*)) case-fatality rates/1000 epileptic patients, injury alone and poisoning alone (Fig. 1(*d*)) case-fatality rates/1000 epileptic patients during the period of 1975–1995. UCD means underlying causes-of-death, CCD means contributory causes-of-death, UCD/CCD means either as underlying or as contributory causes-of-death mentioned in the death certificate.

External causes of injuries (E800–999)

The most frequent specific external cause of injury deaths in epileptic patients was falling, (21.7% during 1975–1986, and 26% during 1987–1995) (see Table 3). Drowning was the other common specific external cause of injury death (9 and 10%, respectively during the two periods). Accidental poisoning was a relatively frequently employed code during the first study period (30 cases, 16%), but was used less frequently in the second (five cases, 2%). All these cases belonged to the group of accidental poisoning

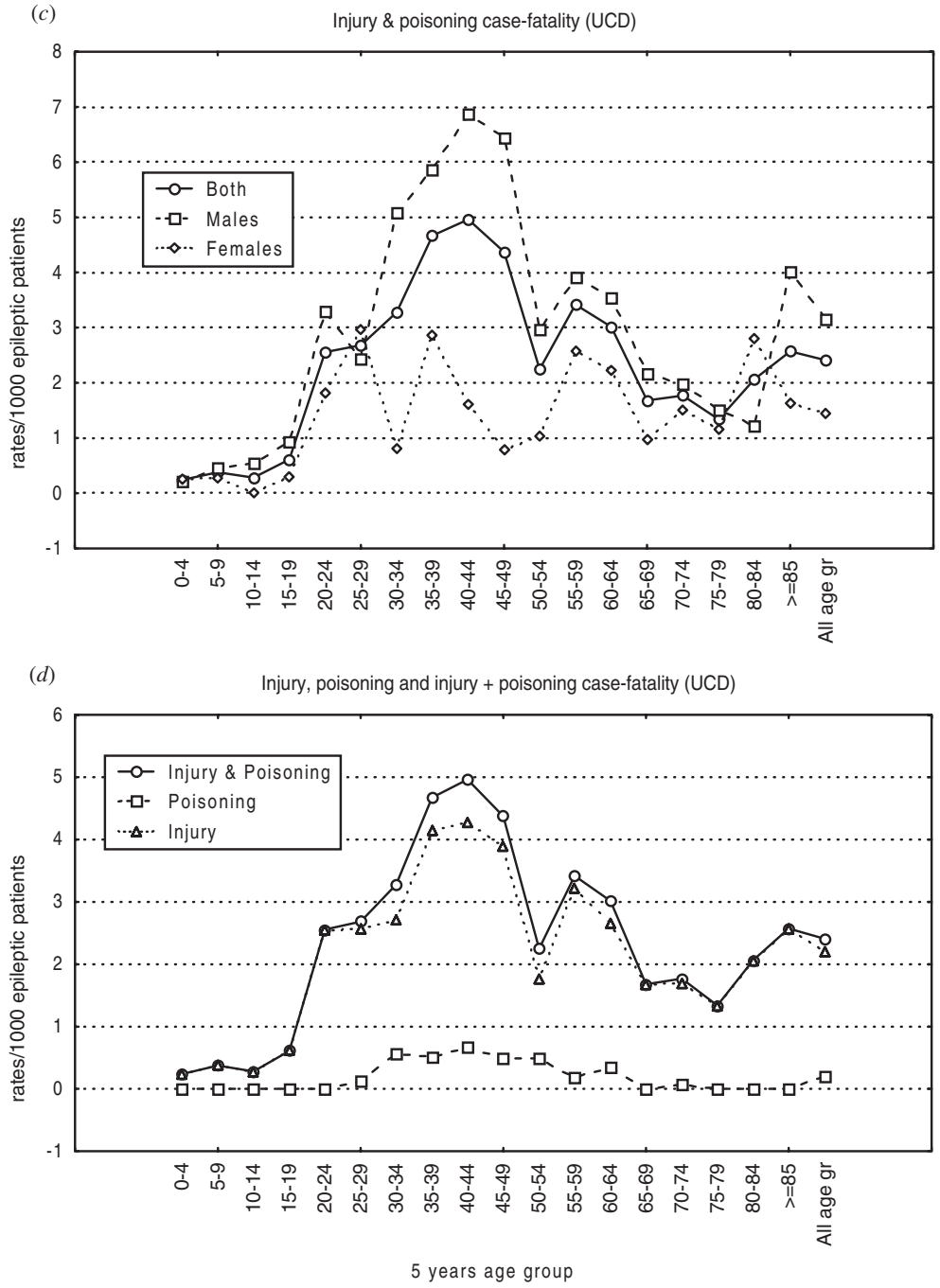

Fig. 1: (Continued)

by alcohol not elsewhere classified (E860). Transport-related deaths were few in number, a total of 11 cases.

DISCUSSION

A significant excess of deaths due to injury or poisoning has been observed among persons with epilepsy in retrospective studies[23–25]. Incidence rates have been found to vary between 5 and 11%, compared with 5.8% in our nationwide study. Further, in one Swedish metropolitan area an excess mortality rate (SMR 5.6) due to injury and poisoning was observed[7]. However, limitations of this study resulting from misclassification and under-reporting have been mentioned.

Epilepsy has been shown to be under-reported on death certificates[23,24], and approximately 20% of other disorders are misclassified as epilepsy[7,39–43]. The death certificates of patients with epilepsy do

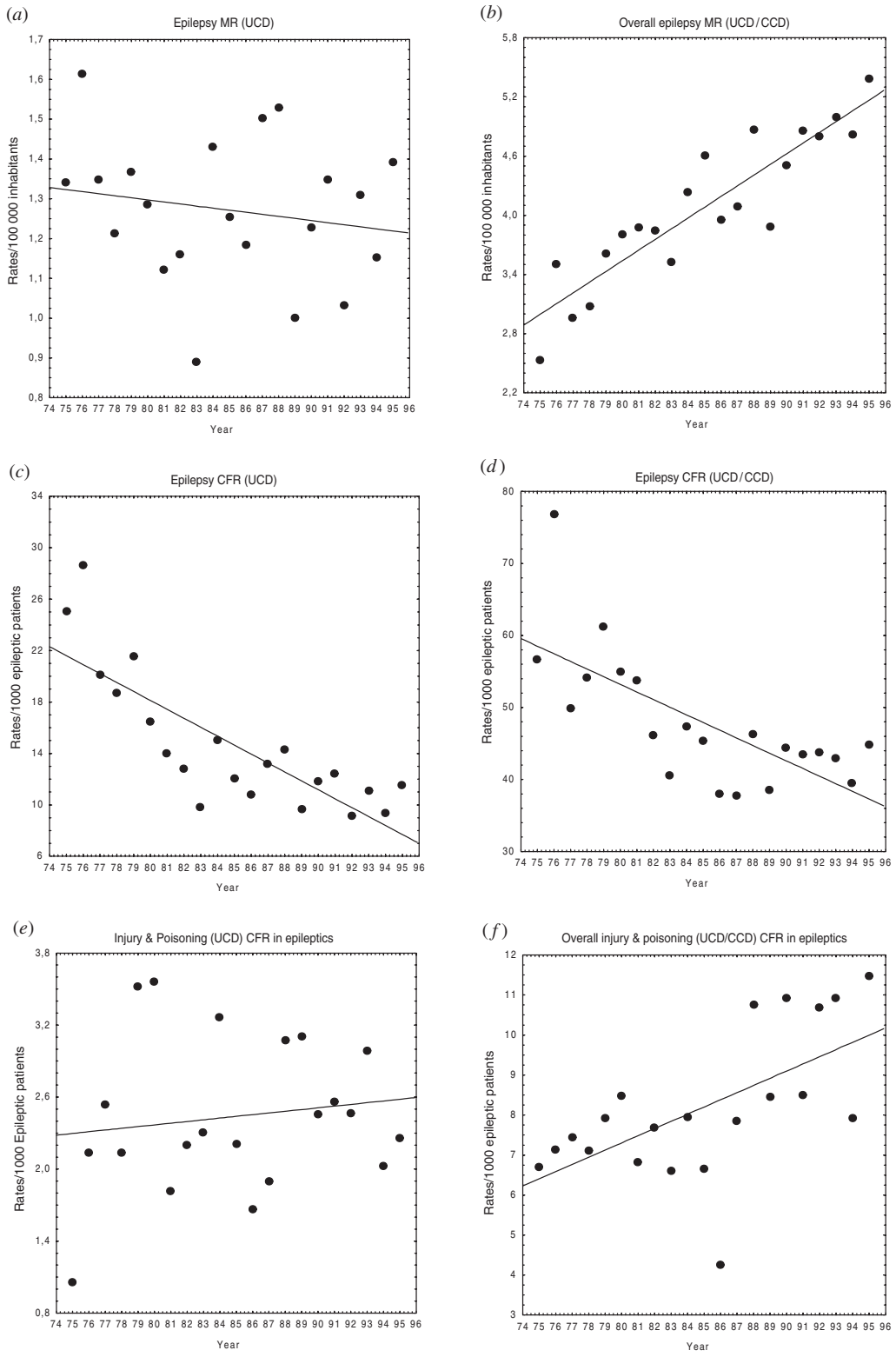

Fig. 2: Scatterplot and trend line of various age adjusted mortality and case fatality rates in relation to time. UCD = underlying causes-of-death, CCD = contributory causes-of-death, UCD/CCD = either as underlying or as contributory causes-of-death mentioned in the death certificate. MR = mortality rates, CFR = case-fatality rates. (*a*) Epilepsy mortality rates/100 000 inhabitants where epilepsy was coded as UCD. (*b*) Overall epilepsy mortality rates/100 000 inhabitants where epilepsy was coded either as UCD or as CCD. (*c*) Epilepsy case fatality rates/1000 epileptic patients where epilepsy was coded as UCD. (*d*) Overall epilepsy case fatality rates/1000 epileptic patients where epilepsy was coded either as UCD or as CCD. (*e*) Injury and poisoning case fatality rates/1000 epileptic patients where injury was coded as UCD. (*f*) Injury and poisoning case fatality rates/1000 epileptic patients where injury and poisoning was coded either as UCD or as CCD.

Table 1: National mortality trend in Sweden during 1975–1995 per 100 000 inhabitants and per 1000 epileptics.[a] Summary of regression analysis.

Mortality variables	R^2	Beta	St. err. of beta	B	St. err. of B	$t(19)$	P-level
Epilepsy (UCD) mortality rates/100 000 inhabitants	0.03	−0.18	0.23	−0.01	0.01	−0.80	0.435
Epilepsy mortality (UCD/CCD) rates/100 000 inhabitants	0.82	0.91	0.10	0.11	0.01	9.35	<0.005
Epilepsy (UCD) case-fatality rates/1000 epileptics	0.65	−0.81	0.14	−0.7	0.12	−5.99	<0.005
Epilepsy (UCD/CCD) case-fatality rates/1000 epileptics	0.50	−0.71	0.16	−1.06	0.24	−4.38	<0.005
Injury & poisoning (UCD) mortality rates/1000 epileptics	0.02	0.14	0.23	0.01	0.02	0.61	0.546
Injury & poisoning (CCD) rates/1000 epileptics	0.53	0.73	0.16	0.30	0.07	4.66	<0.005
Injury & poisoning mortality(UCD/CCD) /1000 epileptics	0.37	0.61	0.18	0.18	0.05	3.35	<0.005

[a] Year of data was the independent variable and various mortality rates were dependent variables.

Table 2: Number and proportions (U/U + C) of underlying (U) and contributory (C) causes-of-death in Sweden[a] during the period between (a) 1975–1980 and 1981–1986, (b) 1975–1980 and 1981–1995.

	1975–1980 Number (Proportion)	1981–1986 Number (Proportion)	1981–1995 Number (Proportion)	Difference between 1975–1980 & 1981–1986		Difference between 1975-1980 & 1981–1995	
				Proportion	Percentage	Proportion	Percentage
Epilepsy							
Underlying	638 (0.437)	574 (0.302)	1567 (0.285)	−0.13	−31	−0.152	−35
Contributory	823	1324	4923				
Underlying/contributory	1461	1898	5497[b]				
Injury & poisoning							
Underlying	83 (0.349)	103 (0.35)	322 (0.285)	0.001	0.29	−0.064	−18
Contributory	171	210	1048				
Underlying/contributory	238[b]	294[b]	1132[b]				

[a] Only cases mentioned together with epilepsy and injury as contributory causes of death and vice versa.
[b] For injury and poisoning some cases were mentioned in both category (U & C) in ICD-8 (1975–1986) and in ICD-9 (1987–1995), for epilepsy some cases were mentioned in both category in ICD-9.

not always have epilepsy listed upon them, mainly because the certifying physician is not aware of the patients past medical history. In one study epilepsy was found to be listed in only 29% of the death certificates of epileptics[23]. However, in cases subject to post-mortem examination there seems to be a preference to count death from epilepsy, alongside accidental and self-inflicted deaths, as suicides, particularly in younger age groups[42].

In our study all conditions mentioned on each death certificate were included. Epilepsy and injury diagnoses were separated according to their status as underlying, contributing or multiple cause-of-death. Among cases where epilepsy was mentioned as an UCD, injury or poisoning was mentioned in 20.5% of cases as a contributory cause. Accordingly, it can be questioned whether the sequences of events reported on the death certificates of epileptics are correctly described. It may well be that injury is substantially under-reported as an UCD. We do not know the reporting practice regarding UCD, i.e. have information bearing on the correctness of statements concerning the condition that initiated the train of events leading to death. For all fatalities where injury resulted from seizure, an injury should be coded as an UCD. There are two possible ways of reporting cases where epilepsy contributes directly to death—status epilepticus and sudden unexpected death. Among all seizure-related accidents leading to a fatal injury, the injury should be coded as an UCD, and the epileptic seizure as a contributory cause. Unfortunately, our study design did not permit any specific analysis of reporting errors. However, the influence on trend of the adjustment in registration practice for the Swedish cause-of-death registry seems to be of major importance.

Changes in registration practice may have a profound influence on published cause-of-death statistics. It can be seen that, prior to 1981, coders at Statistics Sweden had a greater tendency to select epilepsy or injury and poisoning as UCD. Later, other diagnoses were more common. It is not always easy to assess the importance of registration practice in relation to other factors. Examples of such factors are: (i) changes in the natural histories of diseases; (ii) altered diagnostic criteria; (iii) altered treatment methods; (iv) altered reporting habits among physicians; and (v) measures to prevent disease and injury.

Among all cases, independent of injury outcome, we observed that 24% (97/400) were due to falls

Table 3: Number of deaths according to external (E-code) and natural (N-code) causes of injury in patients with epilepsy during 1975–1995.

N-code 1975–1986	Traffic related E807–846	Poisoning E859–877	Fall E880–887	Burns E890–899	Nature & environment E900–909	Drowning E910	Other E911–939	Late effect E940–949	Suicide E950–959	Homicide E960–969	Intention undetermined E980-989	Totals E800–999
Fracture	0	0	23	0	0	0	0	3	0	0	3	29
ICIEF[a]	1	0	15	0	0	0	6	26	0	1	5	54
IITA[b]	0	0	0	0	0	0	0	0	0	0	1	1
Open wound	0	0	1	0	0	0	0	0	0	0	0	1
FBEO[c]	0	0	0	0	0	0	7	0	0	0	0	7
Poisoning	0	0	0	0	0	0	0	0	2	0	16	18
TENMS[d]	0	30	0	2	0	0	0	0	0	0	7	39
Unspecified	2	0	1	0	1	17	1	0	5	0	6	33
All groups	3	30	40	2	1	17	14	29	7	1	38	182
N-code 1987–1995	E800–848 excluding 830, 832	E850–869	E880–888	E890–899	900–909	E830, 832, 910	E911–928	E929	E950–959	E960–969	E980–989	Totals E800–999
Fracture	1	0	31	0	0	0	0	0	0	0	1	33
ICIEF	4	0	25	0	0	0	13	1	0	1	2	46
IITA	2	0	1	0	0	0	0	0	0	0	1	4
Late effect IP[e]	0	0	0	0	0	0	0	32	0	2	2	36
Crushing injury	1	0	0	0	0	0	0	0	0	0	0	1
FBEO	0	0	0	0	0	0	12	0	0	0	0	12
Burns	0	0	0	1	1	0	0	0	0	0	0	2
Unspecified	0	0	0	0	4	22	2	0	1	0	9	38
Poisoning	0	0	0	0	0	0	0	0	10	0	16	26
TENMS	0	5	0	0	0	0	0	0	1	0	14	20
All groups	8	5	57	1	5	22	27	33	12	3	45	218

[a] ICIEF, intracranial injury excluding fracture; [b] IITA, internal injury to thorax and abdomen; [c] FBEO, foreign bodies entering through orifices; [d] TENMS, toxic effect of non-medicinal substances; [e] IP, injury and poisoning.

(Table 3). No information was available to explore specific circumstances in relation to fall accidents. Fatal risks are mostly connected with falls from the same or higher levels (ladders, etc.). However, people with epilepsy are also at an increased risk of falls not directly related to a seizure[33,34]. Balance disturbances and ataxia are common adverse effects of antiepileptic drugs[35], and eight new antiepileptic medications were licensed worldwide in the 1990s[5,18]. A follow-up of the total impact on fall injuries of new drug therapies, focussing on total response, is therefore recommended[45].

Most head injuries have been found to be the result of fall accidents. We observed 41% of intracranial fatal injuries among fall accidents (40/97 cases) and 36% among traffic accidents (5/11 cases). Among all fatalities, skull fractures and intracranial injuries predominate[28]. However, among all head injuries in relation to seizures, only a few are life threatening[28–30], but severe head injuries are associated with a substantially increased risk (SIR 17.0) of epilepsy[44].

Drowning has been reported to occur mostly among young people, with a mean age of 20.5 years[25]. The corresponding figure in our study was 39 years. Drowning is also reported as the most common cause of fatal outcome in children with epilepsy[26]. In a Norwegian study, 11 of 14 child fatalities were found to be due to drowning[25]. However, the deaths of only three children with epilepsy in our study (3/65, 4%) were due to drowning. The lack of proper (constant) supervision when using bathtubs, swimming pools, or in connection with recreational swimming can explain most of the fatalities[27]. Compared with all fatalities among children aged 0–14 years, epilepsy was mentioned in 65 cases as an underlying cause (65/183, 35.5%). A separate analysis of epileptic children has therefore been initiated.

One large group of fatalities consisted in cases of poisoning, 16% during the period 1975–1985, and 2% during 1986–1995. The significant reduction is probably explained by change from ICD-8 to ICD-9. The number of cases of unintentional and undetermined causes due to poisoning decreased during the latter period (Table 3).

Between 12 and 16% of the injuries among epileptic patients are due to burns[9,15]. Most severe burns requiring medical care occur in connection with cooking, showering and room heaters[31,32]. In our study fatal burn injuries seem to be of limited importance. Only three patients died as a result of burn injury during the study period.

Studies of suicides among persons with epilepsy show inconsistent results. Some have demonstrated a two- to 10-fold increase in suicide rate[23,36], but this finding has not been confirmed by others[24,37,38]. The difference between observed and expected numbers of suicide deaths was found to be 3.5 in one Swedish metropolitan area, and the corresponding figure for cases with undetermined cause was 11.1[7]. The statistical methods used, which included comparisons on proportional mortality rates between two different populations, has been questioned[7]. In several cases, a fatal injury could not be determined as unintentional or purposely inflicted. In our study, 19 deaths (5%) were classified as suicide. However, in 83 cases (21%) it could not be decided whether death resulted from an accident or an intentional act. The relationship to poisoning from alcohol is of interest in this context, but prospective large population-based studies with good diagnostic accuracy, and better prospects of determining cause-of-death are recommended[42].

CONCLUSIONS

Epilepsy mortality (as an UCD) has not changed significantly over the last two decades in Sweden. However, overall mortality (where epilepsy was coded either as an underlying or contributory cause-of-death) in patients with epilepsy increased significantly over the same period. The coding of injury and poisoning as a contributory cause-of-death among persons with epilepsy increased during the study period. Intracranial fatal injuries in connection with fall accidents predominate, especially among elderly persons. However, the proportion of each diagnostic group as an underlying cause decreased by 35% for epilepsy, and by 18% for injury and poisoning from 1981 and onwards. In general, the change of Swedish registration practice meant closer adherence to instructions included in the ICD. Differences in the application of the ICD rules may mean that a condition selected as UCD in one country might be regarded as a contributory cause in another. It is concluded that any epidemiologist working with international cause-of-death statistics should, if possible, analyse both underlying and contributing cause. There is scope for national adaptations, but there is at present no mechanism for coordination of instructions between nations. Comparing cause-of-death statistics from different countries remains a hazardous exercise, and both underlying and contributing cause-of-death statistics should be considered in analyses of mortality trends.

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